

WHAT IS CLAIMED IS:

1. A method for treating a connective tissue disorder which comprises:
 - a) generating a recombinant vector that comprises one or more DNA sequences encoding one or more genes of interest;
 - b) infecting a population of *in vitro* cultured target cells with said recombinant vector, resulting in a population of transduced target tissue cells; and,
 - c) transplanting said transduced target cells to the mammalian host, such that subsequent expression of said gene or genes within the host reduces at least one deleterious joint pathology or indicia of inflammation normally associated with a connective tissue disorder; wherein said gene of interest encodes one or more therapeutic genes selected from the group consisting of: interleukin-1 receptor antagonist protein; a Lac Z marker gene; soluble IL-1 receptor; soluble TNF- α receptor, a proteinase inhibitor; a cytokine; CTL-A₄; FasL; and biologically active derivatives or fragments of these genes.
2. The method of Claim 1, wherein said target cell is selected from the group consisting of connective tissue cells and non-connective tissue cells.
3. The method of Claim 2, wherein said connective tissue cells are selected from the group consisting of synovium, cartilage, tendon, ligament, skin, bone, meniscus, and intervertebral disc cells and said non-connective tissue cells are selected from the group consisting of hematopoietic progenitor cells, stromal cells, bone marrow cells, myoblasts, leukocytes, lymphoid cells and myeloid cells.

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4. The method of Claim 3, wherein said transduced target cells are transplanted at one or more locations selected from the group consisting of a joint space, bone marrow or blood stream of said host.

5. The method of Claim 2, wherein said cytokine is one or more members selected from the group consisting of IL-4, IL-10, IL-13, growth factor, and BMP.

6. The method of Claim 5, wherein said BMP is selected from the group consisting of BMP-1, BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-7, BMP-8 and BMP-9.

7. The method of Claim 6, wherein said BMP is selected from the group consisting of BMP-2 and BMP-7.

8. The method of Claim 2, wherein said cytokine is vIL-10.

9. The method of Claim 2, wherein said cytokine is growth hormone.

10. The method of Claim 5, wherein said growth factor is selected from the group consisting of IGF, FGF and TGF.

11. The method of Claim 10, wherein said growth factor is selected from the group consisting of IGF-1 and IGF-2.

12. The method of Claim 2, wherein said soluble IL-1 receptor is selected from the group consisting of soluble IL-1 receptor Type I and soluble IL-1 receptor Type II.

13. The method of Claim 2, wherein said soluble TNF- α receptor is selected from the group consisting of soluble TNF- α receptor Type I and soluble TNF- α receptor Type II.

14. The method of Claim 2, wherein said proteinase inhibitor is selected from the group consisting of TIMP-1, TIMP-2, TIMP-3, TIMP-4, PAIs and serpins.

15. The method of Claim 2, wherein said recombinant vector is selected from the group consisting of a viral vector and a non-viral vector.

16. The method of Claim 3, wherein said connective tissue cells are synovial cells.

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SUP C2)

500 c3) 17. The method of Claim 15, wherein said recombinant vector is a viral vector selected from the group consisting of an adenovirus, an adeno-associated virus, a herpes virus and a retrovirus.

18. The method of Claim 17, wherein said retroviral vector is selected from the group consisting of MFG and pLJ.

19. The method of Claim 15, wherein said recombinant vector is a plasmid DNA vector.

20. The method of Claim 2, wherein transplantation of transduced target cells is by intraarticular injection.

21. The method of Claim 16, wherein said synovial cells are autologous synovial cells.

500 c4) 22. The method of Claim 18, wherein the retroviral vector is an MFG vector and the gene is selected from the group consisting of sIL-1R Type I, sIL-1R Type II, sTNF- α R Type I, sTNF- α R Type II, CTLA4, FasL, BMP-2, BMP-7, IGF-1, IGF-2, vIL-10, TIMP-1, TIMP-2, TIMP-3, TIMP-4, PAIs, serpins, IL-4, IL-10 and IL-13.

23. The method of Claim 22, wherein the gene is selected from the group consisting of sIL-1R Type I, sIL-1R Type II, sTNF- α R Type I and sTNF- α R Type II.

24. The method of Claim 22, wherein the genes used are both sIL-1R and sIL-1R.

25. The method of Claim 22, further including the step of storing said population of transduced target cells prior to transplantation.

26. The method of Claim 25, wherein said population of transfected connective cells are stored in 10% DMSO under liquid nitrogen prior to transplantation.

27. A method for treating a connective tissue disorder, comprising:

introducing one or more DNA sequences encoding one or more genes of interest into at least one target cell of a host by employing non-viral means selected from the group consisting of liposome, calcium phosphate, electroporation, DEAE-dextran and injection of naked DNA such that subsequent expression of said gene or genes within said host reduces at least one deleterious

joint pathology or indicia of inflammation normally associated with a connective tissue disorder;

wherein said gene of interest is one or more therapeutic genes selected from the group consisting of IRAP; a LacZ marker gene; sIL-1R; sTNF- α R, a proteinase inhibitor; a cytokine; CTLA4; FasL; and biologically active derivatives or fragments of these genes.

28. The method of Claim 27, including employing a liposome selected from the group consisting of CD-cholesterol and SF-cholesterol.

29. A method to produce an animal model for the study of joint pathologies which comprises:

a) generating a recombinant vector that contains one or more DNA sequences encoding one or more genes of interest; or biologically active derivatives or fragments thereof;

b) infecting a population of *in vitro* cultured target cells with said recombinant vector, resulting in a population of transduced target cells; and,

c) transplanting said transduced target cells to a mammalian host;

wherein said gene is one which induces one or more symptoms of a joint pathology.

30. The method of Claim 29, wherein said target cell is selected from the group consisting of connective tissue cells and non-connective tissue cells.

31. The method of Claim 30, wherein said gene is selected from the group consisting of IL-1 α ; IL-1 β ; IL-2; IL-8; IL-12; IL-15; IL-17; TNF- α ; TNF- β ; gelatinase; stromelysin; collagenase; aggrecanase; iNOS; and biologically active derivatives or fragments of these genes.

32. The method of Claim 31, wherein said recombinant vector is selected from the group consisting of viral vectors and non viral vectors.

33. The method of Claim 32, wherein said viral vector is selected from the group consisting of adenovirus, adeno-associated virus, herpes virus and retrovirus.

34. The method of Claim 33, wherein said retroviral vector is selected from the group consisting of MFG and pLJ.

35. The method of Claim 32, wherein said recombinant vector is a plasmid DNA vector.

36. The method of Claim 29, wherein transplantation of transduced target cells is by intraarticular injection.

37. The method of Claim 30, wherein said connective tissue cells are selected from the group consisting of synovium, cartilage, tendon, ligament, bone, bone marrow, skin, meniscus and intervertebral disc cells, and said non-connective tissue cells are selected from the group consisting of hematopoietic progenitor cells, stromal cells, bone marrow cells, myoblasts, leukocytes, lymphoid cells and myeloid cells.

38. The method of Claim 37, wherein said connective tissue cells are synovial cells.

39. The method of Claim 38, wherein said synovial cells are autologous synovial cells.

40. The method of Claim 34, wherein said recombinant retroviral vector is MFG and said gene is selected from the group consisting of human IL-1 α ; human IL-1 β ; TNF- α , and biologically active derivatives or fragments thereof.

41. The method of Claim 35, wherein said recombinant plasmid DNA vector is CMV-IL-1 β .

42. The method of Claim 17, including employing a high titer concentration of retroviral vector.

43. The method of Claim 33, including employing a high titer concentration of retroviral vector.

44. The method of Claim 29, wherein said transduced target cells are transplanted at one or more locations selected from the group consisting of a joint space, bone marrow or blood stream of said host.

ADD (6)